



Case report

Toxicokinetics of cocaine and metabolites in a body-packer becoming symptomatic

Philippe Hantson MD, PhD Professor*, Arnaud Capron PhD Doctor, Pierre Wallemacq PhD Professor

Louvain Centre for Toxicology and Applied Pharmacology, Université catholique de Louvain, Brussels, Belgium

ARTICLE INFO

Article history:

Received 11 April 2011

Received in revised form

16 June 2011

Accepted 20 July 2011

Available online 9 August 2011

Keywords:

Body-packer

Cocaine

Metabolites

Toxicokinetics

ABSTRACT

Life-threatening complications may occur in body-packers and the rupture of a single packet containing cocaine may lead to fatality. We report the case of a 35-year-old body-packer who developed at the airport clinical signs of cocaine toxicity. There was evidence of bowel obstruction. The plasma concentration of cocaine, benzoylecgonine (BZE) and ecgonine methyl ester (EME) was determined 1 h after symptoms onset, during surgery and postoperative period. The measured peak value at 1 h was 594 ng/ml for cocaine, 9423 ng/ml for BZE and 3261 ng/ml for EME. We confirm the following order BZE > EME > cocaine for peak plasma concentrations. A rebound in plasma levels was found during surgery, together with electrocardiographic changes. A total of 107 packets were eliminated, and the patient survived.

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1. Introduction

The term “body-packers” usually refers to persons who have ingested cocaine or heroin-filled packets in the course of international drug traffic. An increasing number of body-packers are arrested at the airports. They are usually carrying 50 to 120 packets weighing 8–10 g each. The packets can be seen radiographically, but coprostasis can disturb accurate diagnosis. When the body-packer is asymptomatic, the treatment is based on the administration of mild laxatives and on evacuation of packets by bowel irrigation.¹ Symptoms of abdominal pain and vomiting indicate gastrointestinal obstruction. This obstruction may cause the absorption of cocaine through the semi-permeable packets, with an increasing of rupture eventually causing intoxication and death by cardiac arrest. The incidence of bowel obstruction is approximately 5%. When severe intoxication occurs, the mortality rate may be as high as 68% and the intraluminal rupture of a single packet may be fatal.² Immediate laparotomy is indicated in case of high suspicion of rupture.^{2,3} There are relatively few *in vivo* data regarding the toxicokinetics of cocaine and its metabolites in body-packers who develop clinical symptoms and require surgical management.⁴ We describe here a case with serial determination of plasma concentrations of cocaine and its metabolites.

2. Case report

A 35-year-old man (90 kg weight), non cocaine abuser, arrived at the airport after a 16-hours transatlantic flight coming from South-America. He presented in the security area with abdominal pain and vomiting, and was found extremely agitated. The police suspected that he was a body-packer and called the emergency mobile unit. The patient remained extremely agitated, despite diazepam administration by the medical rescuers, but did not present seizures. Vital signs were: arterial blood pressure 190/110 mm Hg, heart rate 140/min, respiratory rate 34/min, axillary temperature 36.5 °C. The abdomen was diffusely tender and no abdominal sounds were audible. Due to the suspicion of ruptured cocaine packets, he was referred to the university hospital. At arrival in the intensive care unit (ICU), 1 h after the first clinical symptoms, he was still extremely agitated despite the continuous infusion of 400 mg/h of propofol; the pupils were dilated bilaterally. He was breathing spontaneously and had an arterial blood pressure of 200/120 mm Hg (mean 131 mm Hg). The electrocardiogram (ECG) revealed sinus tachycardia with flat T waves in the anterior leads. The abdomen computed tomography (CT) revealed the presence of numerous packets starting from the stomach to the rectum. There were no signs of bowel perforation. Serum creatinine was 1.86 mg/dl (0.60–1.30), CK 1153 IU/l (<400), CK-MB 6.8 µg/l (<3.5). Due to the clinical signs of cocaine intoxication and the suspicion of bowel obstruction, an urgent laparotomy was decided. Thirty packets were removed through the gastric incision, while 70

* Corresponding author. Department of Intensive Care, Cliniques St-Luc, Avenue Hippocrate, 10, 1200 Brussels, Belgium. Tel.: +32 2 7642755; fax: +32 2 7648928.
E-mail address: philippe.hantson@uclouvain.be (P. Hantson).

packets were extracted by a caecal opening; seven packets were additionally removed from the rectum by anal dilatation. At inspection, there was however no evidence for rupture. The patient remained stable hemodynamically during the surgical procedure that lasted 4 h; there was a brief episode of ST segment depression at the beginning of surgery. The postoperative course was uneventful. The packets were confiscated by the authorities. We were informed that only cocaine was present in the packets, with a total weight of 1350 g.

2.1. Method

Blood was sampled on lithium heparin as an anticoagulant. In order to minimize cocaine hydrolysis or degradation, plasma and urine samples were kept at 4 °C for a maximum of 12 h before cocaine testing. Quantification of cocaine and its metabolites was performed using a liquid chromatographic (LC) system coupled with a tandem mass spectrometer (MS) as detector. Drugs were extracted from 200 µL of plasma or urine, at pH 8.9 using a mixture of chloroform/2-propanol (v/v; 9/1). Organic layer was evaporated to dryness and dried extract was reconstituted with 200 µL of acetonitrile and transferred into vials for LC–MS/MS analysis (Table 1).

3. Discussion

Bowel obstruction and symptoms of cocaine intoxication are clear indications for surgery in body packing patients.² Our patient had developed tachycardia with electrocardiographic changes, arterial hypertension and extreme agitation as main symptoms. Benzodiazepines appear to be the drug of choice to treat agitation and prevent seizures. When they are ineffective, other sedative-hypnotic drugs may be chosen. Propofol is FDA approved for general anesthesia, monitored anesthesia care sedation and sedation for mechanically ventilated patients in the ICU. The maintenance dose for a monitored anesthesia care sedation is usually 1.5–4.5 mg/kg/h intravenously. Propofol is extensively metabolized in the liver by cytochrome P450 2B6 and has a high metabolic clearance suggesting extra-hepatic metabolism. There is no description of metabolic interactions between propofol and cocaine. High doses of propofol will produce central nervous system depression, but will not fully protect against cocaine-induced seizures. Due to cocaine-induced psychosis, this patient tolerated higher doses while maintaining spontaneous breathing. Patients receiving such dosage regimen should be continuously monitored.

Table 1
Toxicokinetic data in plasma and urine.

Plasma		Cocaine	Benzoylcegonine	Ecgonine methyl ester
Time	Event	(ng/mL)	(ng/mL)	(ng/mL)
2:30 pm	ICU, 1 h after first symptoms	594	9423	3261
4:15 pm	Start of surgery	117	5899	1671
4:34 pm	Transient ECG changes	340	7862	2477
6:00 am	Asymptomatic, postoperative	46	4710	567
Urine				
Time	Sampling			
2:30 pm	Spot	12858	80142	137433
2:30–8:30 pm	6 h-collection (450 ml)	56976	80953	162128
8:30 pm–6:00 am	9 h 30-collection (575 ml)	19999	91299	130075

Most of the toxicokinetics of cocaine and its metabolites in body-packers are usually obtained *post-mortem*. It is generally accepted that the symptoms severity will correlate with blood cocaine concentrations.⁵ This assumption was however challenged by other observations. In cocaine abusers admitted to the Emergency Department, Blaho et al. failed to demonstrate a significant correlation between symptoms and plasma concentrations of cocaine and its metabolites.⁶ Recently, de Prost et al. described the toxicokinetics of cocaine and two metabolites, benzoylecgonine (BZE) and ecgonine methyl ester (EME) in 48-year-old body-packer.⁴ The patient had been admitted asymptomatic to the emergency department. The patient had already evacuated 26 packets of cocaine at the airport, and 54 more packets were eliminated over 2 days following paraffin oil administration. On day 4, he developed signs of cocaine intoxication (tachycardia, hypertension, mydriasis) and ultimately developed seizures and cardiac arrest. He was successfully resuscitated and underwent emergency laparotomy for the removal of 13 more packets; one packet was totally ruptured in the stomach. The determination of plasma concentrations of cocaine, BZE and EME was done 1 h after cardiac arrest and at different times until 30 h. The maximal plasma cocaine and EME concentration was 1660 ng/ml and 2280 ng/ml, respectively. The maximal plasma BZE concentration (10300 ng/ml) was observed at 11 h. The apparent cocaine elimination half-life was 7.6 h. The metabolic ratio was 6.5 for BZE/cocaine and 1.7 for EME/cocaine. Our patient was less severely intoxicated, as he did not present seizures or cardiac arrest. The measured peak plasma concentration for cocaine, BZE and EME was observed 1 h after symptoms onset; the peak value was likely higher at the time the patient was found at the airport. There was a significant rebound of cocaine, BZE and EME concomitant to the ECG changes during the manipulation of the packets contained in the stomach. Furthermore, we confirm that the relative peak concentrations of cocaine are in the following order: BZE > EME > cocaine.^{4,7} BZE is produced both enzymatically by a carboxylesterase-1 or similar enzymes as well as non-enzymatically. EME appears to be formed by plasma and liver butylcholinesterases.

Urine collection has been performed over the 15 h following admission. The main metabolite identified was the EME followed by BZE, and cocaine. Most metabolites concentrations in urine declined below the limits of detection within 48 h.⁸ Generally, about 50% of the ingested dose will be recovered in urine during the 3 days of collection. In the present case report, the cumulated concentrations of all metabolites and parent drug over the 15 h of collection represent a global amount of 0.802 g. Based on the literature, it could be assumed that the body-packer has been exposed to a diffuse absorption of >2 g, explaining the clinical symptoms for a non-chronic cocaine user.⁸

This single observation has obvious limitations. No rupture of any packet could be demonstrated, even if leakage is very likely according to the clinical signs and toxicological data. Due to a limited number of data points, with also a rebound of toxic concentrations, we were not able to determine the apparent elimination half-life of cocaine, BZE and EME. In particular, we can not affirm that there was a strict relationship between the intra-operative electrocardiographic changes and a peak plasma cocaine concentration. Further toxicokinetics analysis is encouraged in body-packers who are symptomatic and survive urgent surgical procedures.

Conflict of interest
None declared.

Funding
None declared.

Ethical approval

None declared.

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